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10/595,076	09/07/2006	Bengt-Ake Bengtsson	05558.0036.PCUS00	2186

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EXAMINER	
BORGHEST, CHRISTINA M	

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1649	

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12/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,076	BENGTSSON, BENGT-AKE	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,8-15,18,25,28-30,33,36 and 37* is/are pending in the application.

4a) Of the above claim(s) *28-30,36 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,8-15,18,25 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's response filed 27 August 2009 is acknowledged. Claims 1, 11 and 12 are amended. Claims 28-30, 36 and 37 remain withdrawn. Claims 1, 2, 5, 6, 8-15, 18, 25 and 33 are under examination.

Rejections withdrawn

Claim Rejections - 35 USC § 112, second paragraph

The rejection of claims 1, 2, 5, 6, 8-15, 18, 25 and 33 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention as set forth at pages 2-3 of the Office action mailed 29 April 2009 is withdrawn in response to Applicant's amendment. Specifically:

(i) Claim 1 has been amended to recite a method for the treatment of a Parkinsonism-Plus Syndrome comprising administration of a substance with a step that clearly relates back to the preamble and identifies a patient population.

(ii) Claim 1 has been amended to recite proper Markush groups.

(iii) Claims 11-12 are have been amended to clarify that hGH is the protein variant referred to in the claims.

Claim Rejections - 35 USC § 112, first paragraph—Written Description

The rejection of claims 1, 2, 6, 8, 10-15, 18, 25 and 33 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as set forth at pages 9-11 of the Office action mailed 29 April 2009 is withdrawn in response to Applicant's amendment of the claims. Specifically, the claims are now limited to treatment with (a) human growth hormone (hGH) or human growth hormone releasing hormone (hGHRH), (b) a variant of (a) that has at least 70% sequence identity thereto and that has agonistic activity on the hGH or hGHRH receptors, respectively (c) and a salt of (a) or (b).

Claim Rejections - 35 USC § 102

The rejection of claims 1, 2, 5, 6, 8, 14, 15, 18, 25 and 33 under 35 U.S.C. 102(b) as being anticipated by Ng et al. (U.S. Patent No. 5,869,452, "the '452 patent—of record) as set forth at pages 11-13 of the Office action mailed 29 April 2009 is withdrawn in response to Applicant's amendment. Specifically, since the instant claims have been amended to be limited to treatment of Parkinsonism-Plus Syndrome, the '452 patent no longer qualifies as prior art.

The rejection of claims 1, 2, 5, 6, 8, 10, 11, 12, 13, 15 and 18 under 35 U.S.C. 102(b) as being anticipated by Bengtsson et al. (U.S. Patent No. 5,736,515, "the '515 patent"—of record) as evidenced by Bauman (Endocrine Reviews, 1991; 12: 424-449—of record) and the AACE Growth Hormone Task Force, Endocrine Practice,

Jan/Feb 2003; 9: 64-76 as set forth at pages 13-15 is withdrawn in response to Applicant's amendment of the claims. Specifically, since the instant claims have been amended to be limited to treatment of Parkinsonism-Plus Syndrome, the '515 patent no longer qualifies as prior art.

The rejection of claims 1, 2, 5, 6, 8, 10-15 and 18 under 35 U.S.C. 102(e) as being anticipated by Johannsson et al. (U.S. Patent No. 6,846,800, "the '800 patent"—of record) as evidenced by Bauman (Endocrine Reviews, 1991; 12: 424-449—of record) as set forth at pages 14-17 of the Office action mailed 29 April 2009 is withdrawn in response to Applicant's amendment of the claims. Specifically, since the instant claims have been amended to be limited to treatment of Parkinsonism-Plus Syndrome, the '800 patent no longer qualifies as prior art.

Claim Rejections - 35 USC § 103

The rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Ng et al. (U.S. Patent No. 5,869,452—the '452 patent—of record) as applied to claims 1, 2, 5, 6, 8, 14, 15, 18, 25 and 33 above and further in view of Goeddel et al. (Nature, 1979; 281: 544-548—of record) as set forth at pages 17-19 of the Office action mailed 29 April 2009 is withdrawn in response to Applicant's amendment of the claims. Specifically, since the instant claims have been amended to be limited to treatment of Parkinsonism-Plus Syndrome, the '452 patent no longer qualifies as a primary reference in an obviousness rejection.

The rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Bengtsson et al (U.S. Patent No. 5,736,515—the '515 patent—of record) as evidenced by Bauman (cited above) and the AACE Growth Hormone Task Force (of record) as applied to claims 1, 2, 5, 6, 8, 10, 11, 12, 13, 15 and 18 above and further in view of Goeddel et al. (Nature, 1979; 281: 544-548—of record) is withdrawn in response to Applicant's amendment of the claims. Specifically, since the instant claims have been amended to be limited to treatment of Parkinsonism-Plus Syndrome, the '515 patent no longer qualifies as a primary reference in an obviousness rejection.

Double Patenting

The rejection of claims 1, 2, 5, 6, 8-15 and 18, 33 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 7,122,515 in view of Bauman (Endocrine Reviews, 1991; 12: 424-449—of record) and further in view of Goeddel et al. (Nature, 1979; 281: 544-548—of record) as set forth at pages 21 and 22 of the Office action mailed 29 April 2009 is withdrawn in response to Applicant's amendment of the claims, which now clearly identify a patient population. Specifically, the claims of the '515 patent encompass methods of treating metabolic syndrome comprising administration of GH and not Parkinsonism Plus Disorders.

Rejection Maintained

Claim Rejections - 35 USC § 112, first paragraph—Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 2, 6, 8, 10-15, 18, 25 and 33 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the amelioration of the symptoms of Multiple Symptom Atrophy or MSA comprising administering to a person suffering from MSA a substance selected from the group consisting of (a) human growth hormone (hGH), (b) a variant of (a) that has at least 70% sequence identity thereto and that has agonistic activity on the hGH receptor, (c) a salt of (a) or (b), wherein administration of said substance ameliorates the symptoms of Multiple Symptom Atrophy or MSA, does not reasonably provide enablement for the claims as broadly recited, as set forth at pages 3-8 in the Office action mailed 29 April 2009, is maintained for reasons of record and the following.

At the outset, it should be noted that Applicant's amendment has overcome a number of the issues raised in the Office action mailed 29 April 2009. Briefly, first, Applicant has amended the claims to delete "prevention." Second, Applicant has amended the claim to delete "a variant of (e) having agonistic activity on the hGHRH receptor and which is encoded by a DNA..." The remaining issues are discussed below.

(i) The remaining issue, which was not addressed in Applicant's Remarks filed 27 August 2009, is that the claims are enabled for amelioration of the symptoms of Multiple

Symptom Atrophy or MSA comprising administering to a person suffering from MSA a substance selected from the group consisting of (a) human growth hormone (hGH), (b) a variant of (a) that has at least 70% sequence identity thereto and that has agonistic activity on the hGH receptor, (c) a salt of (a) or (b), wherein administration of said substance ameliorates the symptoms of Multiple Symptom Atrophy or MSA, does not reasonably provide enablement for the claims as broadly recited, namely "Parkinsonism Plus Syndrome(s) and those syndromes recited in claim 2 or treatment with hGHRH. As noted in the Office action mailed 29 April 2009 at p. 4, Holmberg et al. (Movement Disorders, 2007; 22: 1138-1144—of record) teach that hGH administration in patients with multiple symptom atrophy, or MSA, might decrease symptoms, although results were non-significant (see abstract; p. 1142, Figure 1). The results were equivocal, but suggest that GH therapy might be helpful in the treatment of MSA, thus the art provides some guidance with respect to the ***treatment of MSA with GH***. However, this cautiously hopeful result does not provide support for the enablement of treatment of all Parkinsonism Plus Syndromes. Further, the art is silent with respect to treatment with hGHRH. Further, as noted at p. 5 of the previous Office action, Holmberg state at p. 1143, right column, 2nd and 3rd paragraphs:

> This study is the first to report the effects of GH treatment of patients with MSA. ***As yet, no drug has been shown to reduce progression of MSA.*** (Emphasis added by Examiner). At the time this study was designed, no reliable data were available on spontaneous evolution in MSA patients of the clinical scales used to assess disease progression. Thus, when designing the study, it was impossible to make a reliable sample size calculation for detection of a positive effect. In addition, 37% of the patients discontinued prematurely during the study owing to the aggressive nature of the underlying disease…The results of this study, therefore, suggest that a larger dose of r-hGH could be

> tolerated and may be necessary to demonstrate improvements in patients with MSA.

In other words, the study by Holmberg et al. offers the possibility that GH treatment could lessen symptoms associated with MSA, but also underscore the complexity and the amount of further research that is needed to establish how to treat MSA, not to mention all of the encompassed Parkinsonism Plus Syndromes. Neither the art, nor the specification, provide guidance as to how all of the encompassed Parkinsonism Plus Syndromes can be treated with GH or for that matter whether treatment with hGHRH would be effective. Note also, Mark M (Neurol Clin. 2001; 19: 607-27—of record), which teaches the difficulty in diagnosis and categorization of these different conditions, focusing on Parkinson's disease, dementia with Lewy bodies, MSA, progressive supranuclear palsy (PSP) and corticobasal ganglionic degeneration. Litvan et al. (Arch Neurol. 1997, 54: 937-954—on Applicant's 1449 form) teach that it is difficult to diagnose MSA and that appropriate management of MSA involves an early and accurate diagnosis to allow for the study of treatments to slow the disease process. Like the reference by Holmberg and colleagues, Litvan et al. underscore the lack of predictability and complexity in the art.

(ii) The skilled artisan, when confronting this lack of predictability and complexity must turn to the specification for guidance. The specification provides guidance in the form of a prophetic example of the specific treatment of MSA with GH, and does not address the concerns raised by the Examiner about the treatment of the myriad conditions encompassed by the claims. Given the complexity of the art concerning diagnosis and treatment of Parkinsonism Plus Syndromes, discussed above and

underscored by the teachings cited above, and that the claims are drawn to treatment of this intractable collection of diseases, it would require undue experimentation from one of skill in the art to undertake the empirical testing necessary to establish whether GH or hGHRH are effective.

(iii) As noted at p. 8 of the Office action mailed 29 April 2009, neither the specification, nor the literature suggests that hGHRH (as opposed to GH) would be useful in the treatment of MSA or other Parkinsonism Plus Syndromes and a large quantity of experimentation would be required of the skilled artisan to determine such. Such experimentation is considered undue. The limited guidance in the specification is not adequate and is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

Applicant's remarks focused on variants of GH and hGHRH, but did not address the concerns raised about treatment of any and all Parkinsonism Plus Syndromes, and further, treatment thereof with hGHRH.

Due to the large quantity of experimentation necessary to undertake empirical testing as to whether hGH or hGHRH would be effective in the treatment of any and all Parkinsonism Plus Syndromes, the lack of direction/guidance presented in the specification regarding the same and the absence of working examples directed to the same, the complex nature of the invention and the state of the art, which teaches the intractability of diagnosis and treatment of the encompassed conditions, (the level of skill of those in the art,) and the breadth of the claims with regard to the encompassed

disorders, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649